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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,873	04/27/2001	R. Rao Koganty	042881/0156	7911

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,873	KOGANTY ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *13,15,16,18,23-25 and 28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14,17,19-22,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of the following species: GalNAc as the glycosyl donor; Peptide (L or D) for the platform and natural glycosylation sites is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 13, 15-16, 18, 23-25 and 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicants assert at page 7 of the Remarks that claims 1-14, 17, 19-22, 26-27 and 30-31 reads on the elected species.

Contrary to applicants' assertion the claims that read on the elected species are set forth below. Claim 13, for example does not read on the elected species since this is a peptidomimetic claim i.e., not the elected non-modified peptide.

Status of Claims

Claims 1-31 are pending in the application.

Claims 32-41 have been cancelled in the Preliminary Amendment of 8/3/02.

Claims 13, 15-16, 18, 23-25 and 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

Claims 1-12, 14, 17, 19-22 and 26-27 read on the elected species and are under examination.

Specification

The specification has not been checked to the extent necessary to determine the presence of **all** possible minor errors (grammatical, typographical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Drawings

The drawings are objected to because 1). The specification describes only a Figure 3 but the drawings contain two figures for said Figure 3. Should applicants amend the drawing to show

Fig. 3 as A and B, then the specification must reflect these changes.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 14, 17, 19-22 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mucin 1(MUC1) as the platform and inhibitory activity for a compound in the library, does not reasonably provide enablement for the broadly recited combinatorially-generated library of glycopeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of enabling disclosure provided in the specification is not commensurate with the broad claimed method of generating a library of glycopeptides. The specification

merely provides general statement as to the components that can comprise the glycopeptide library. However, the examples provided therein are drawn to a single glycopeptide i.e., MUC1 as the platform to which a random glycosyl components can be attached. No other platform to which any library of glycosyls can be attached. There is nothing in the specification that discloses the kind, type of residues in the platform that can be randomized. The lack of structure for any of the compounds involve in the generation method made it more difficult to determine the variables involve for making the library. For example, the kind, size, length of platform involve in the glycosylation. Also, the kind of carbohydrates; the number, kind and length of random sites that can be randomly altered, the residues in the platform that can be blocked to prevent its glycosylation. Furthermore, the type of protecting group that can be used and other undefined variables involved in the generation of random glycosylated library of undefined structures. The disclosure does not enable the method of combining the different libraries to produced different levels of libraries. It is not apparent as to what constitute a level library. As applicants recognized, it is important to know the sites of glycosylations as well as the nature and size of the carbohydrates at each site. If one considers the permutations and combinations that arise from all the unique sites and the variety of carbohydrates that may exist on the tandem repeat,

the number of possible arrangements becomes unimaginably large, combinatorial and random techniques result in all of the statistically possible ways in which various reactants can combine without actually identifying any of them until a screening process detects a "hit" for further analysis and identification. Accordingly, to extrapolate the single embodied species of a glycopeptide library to the myriads of libraries produced by the method, including lipid containing glycopeptides would entail undue amount of experimentation. A skilled in the art faces numerous unpredictable factors such as the components of a carbohydrate and/or peptide can be comprised in a library. Others like, the site or amino acid in the peptide that can be modified by attachment of the carbohydrate moieties singly, or in combinations with other components. The different combinations of libraries to constitute the different levels of libraries, the means of attachment, and the type of library that the carbohydrate can assume all entail unpredictable effects or factors. See Ex parte Forman, 230 USPQ 546, BPAI, 1986

Claim Rejections - 35 USC § 112, second paragraph

Claims 1-12, 14, 17, 19-22 and 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 1 is indefinite as it is not clear as to the 'optional " blocking of unreacted glycosylation sites. It would appear that this is not an option during the glycosylation reaction or synthesis. During synthesis the unreacted glycosylation sites have to be positively blocked to prevent unwanted reaction or glycosylation. The "combination" of first level libraries is unclear as to the make up of said composition and/or the standard by which the combination is achieved. It is not clear as to which "***the*** first level" refers to in the preceding step. Also, it is not clear as to which carbohydrate "***the*** carbohydrate" refers back to.

B. The term "higher" in claim 2 is a relative term which renders the claim indefinite. The term "higher" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Furthermore, it is not clear as to which step the "foregoing step" refers to.

C. Non-sequitur for "said peptide" in claims 3 and 4. The base claim does not recite a peptide. "Sited" in claim 6 is misspelled.

D. Claim 11 is indefinite as to what is included or excluded by the term "some", in the context of the claim.

E. Claim 17 is indefinite as to what would be consider "unique" in the context of the claim, especially in the absence of any structural features of the platform. Furthermore, the vicinity of the site fails to describe the residues that are within or outside the vicinity of the site.

F. Claim 27 is indefinite as to what constitutes a "cluster" in the context of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5-12, 14, 17, 19-20, 22 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Vetter et al (WO 95/18971).

Vetter discloses at page 25, line 33 up to page 27, line 10 a method of generating a glycopeptide library of structure Ac-X-X-E (OA)XP-resin, X is any of the 18 side chain protected amino acids as recited therein. The peptide is coupled to a bead (a platform, as claimed). The sequence of reaction and random reapportionment continue until sequences having the desired

lengths are formed. The glycosyl acceptor was produced by deprotecting and activating the side chain of Glu, which is common to each of the molecules. A first set of glycosylating agents e.g., Gal Nac is introduced to the various aliquots of resin beads containing surface reactive functionality to yield a library of glycoconjugates. Aliquots of the original member library were diversified by conjugation to 17 different glycosylamines, inter alia, Gal Nac. See further page 5, summary up to page 7,line 27 and the Examples at pages 38-56. Accordingly, the method steps of Vetter which discloses the same method steps as claimed and using specific compounds fully meet the broad claimed method having no defined structures for the glycopeptide.

Claims 1-2, 5-14, 17, 19-22 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schleyer et al (Angew. Chem. Int.)

Schleyer discloses at page 1976 a method for the generation of a multiple glycopeptides with variation of both sugar and peptide. Schleyer discloses that it is more efficient to couple the sugar directly and stereoselectively to the free hydroxyl groups of amino acid side chains on the resin-bound peptides. Thus, libraries of libraries could be produced by glycosylation of a preformed peptide library. See specifically the reaction schemes. Therefore, the specific method steps of Schleyer

employing specific components therein fully meet the broad claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-14, 17, 19-22 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao (U.S. 5,795,958). Rao discloses at col.7, line 60 up to col. col. 11,line 45 discloses a method of generating a library of glycosylated peptide comprising separately introducing a set of first amino acids to each aliquots of the solid phase support; the amino acids used for peptide synthesis are the base-labile (Fmoc) (protected group, as claimed) amino acids, completely coupling

the amino acids to substantially all of the sites of the solid phase support to form a solid phase support/new subunit combination; assessing the completeness of coupling and, if necessary, forcing the reaction to completeness; thoroughly mixing the aliquots of the solid phase support/new subunit combination; and, after repeating steps (a)-(e) the desired number of times, a final step of (f)removing the protecting groups such that the bio-oligomer remains linked to the solid phase support. Complete coupling will result in solid phase support/first amino acid combinations. Generally, The method of the present invention may also be used with the Boc-amino acids. In addition, the method of the invention can be used with other N-alpha. -protecting groups that are familiar to those skilled in this art. Rao discloses an N-terminal amino acid e.g., a serine to which a carbohydrate is o-glucosidically linked (i.e., a glycopeptide, as claimed) or the penultimate amino acid to which carbohydrate is o-glucosidically linked. The bio-oligomer collection or library may comprise peptides. Rao discloses that the carbohydrate is fucose. Rao fails to disclose a glycosyl. However, Rao discloses in the prior art discussion the glycosyl peptide preparation by random synthesis citing e.g., Peters et al., 1992, J. Chem. Soc. Perkin Trans 1:1163-1171. Rao discloses that a library or collection of peptides would combine the

flexibility and ease of the screening of a random peptide library, with the specificity offered by the attachment of peptide scaffolding to a critical carbohydrate residue. It would have been obvious to one having ordinary skill in the art to use other carbohydrates in the method of Rao, e.g., glycosyl if a particular carbohydrate is the desired glycopeptide. Rao discloses the advantage, in general, of a glycopeptide. This will provide the motivation to one having ordinary skill in the art in making a glycopeptide library.

Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vetter or Rao or Schleyer in view of Ding et al (Cancer Immunology Immunotherapy).

Each of Vetter or Rao or Schleyer does not describe the glycopeptide having the structure as recited in claim 3 or its fragment as in claim 4 (i.e., MUC1). However Ding discloses in the abstract that various synthetic peptides of the formula as recited induces high IgG responses. These synthetic MUC 1peptide could be used both prophylactically and therapeutically to inhibit the growth of MUC1-transfected tumor cells and prolong the survival of tumor-bearing mice. Accordingly, one having ordinary skill in the art would be motivated to prepare MUC1 peptide in the method of any one of Vetter, Rao or Schleyer

since these peptides have therapeutic and prophylactic effect as taught by Ding above.

No claim is allowed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Longenecker discloses a MUC-1 as an immunosuppressant.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-7924.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
December 11, 2003